

Claims

What is claimed is:

1. A composition comprising:
  - (a) a first polynucleotide comprising:
    - (1) a gene switch/biosensor comprising a nucleic acid sequence encoding a physiological stimulus-sensitive chimeric transactivator, and
    - (2) an operatively linked tissue-specific promoter; and
  - (b) a second polynucleotide comprising a nucleic acid sequence encoding a stem cell-attracting chemokine.
2. The composition of claim 1, wherein said physiological stimulus-sensitive chimeric transactivator is oxygen-sensitive and comprises a GAL4 DNA-binding domain (DBD), a oxygen-dependent degradation domain (ODD), and a p65 activation domain (p65 AD); and wherein said second polynucleotide further comprises a GAL4 upstream activating sequence (UAS) linked to said nucleic acid sequence of said second polynucleotide, and wherein in response to hypoxia, said transactivator binds to the GAL4 UAS, resulting in expression of said nucleic acid sequence encoding said stem cell-attracting chemokine.
3. The composition of claim 1 or 2, wherein said tissue-specific promoter is specific for expression in a tissue selected from the group consisting of kidney, epithelial tissue, endothelial tissue, liver, brain, neural tissue, thymus, and pancreas.
4. The composition of any of claims 1 to 3, wherein said tissue-specific promoter is selected from the group consisting of CLCN5, rennin, androgen-regulated protein, sodium-phosphate cotransporter, renal cytochrome P-450, parathyroid hormone receptor, kidney-specific cadherin, E-cadherein, estrogen receptor (ER) 3, endoglin, ICAM-2, human phenylalanine hydroxylase (PAH), human C-reactive protein (CRP), human enolase (ENO3), thy-1 antigen, gamma-enolase, glial-specific glial fibrillary acidic protein (GFAP), human FGF1, GATA transcription factor, and pancreas duodenum homeobox 1 (PDX-1).

5. The composition of claim 1 or 2, wherein said tissue-specific promoter is a cardiac-specific promoter.

6. The composition of any of claims 1 to 3, wherein said tissue-specific promoter is a cardiac-specific promoter selected from the group consisting of the ventricular form of the MLC-2v promoter, a fragment of the native MLC-2v promoter, alpha myosin heavy chain promoter, and myosin light chain-2 promoter.

7. The composition of any of claims 1 to 4, wherein said stem cell-attracting chemokine is selected from the group consisting of SCF, vascular endothelial growth factor (VEGF), granulocyte colony-stimulating factor (G-CSF), an integrin, and hSDF-1alpha.

8. The composition of any of claims 1 to 4, wherein said stem cell-attracting chemokine comprises hSDF-1alpha.

9. The composition of any of claims 1 to 4, wherein said physiological stimulus is associated with cell injury.

10. The composition of any of claims 1 to 4, wherein said physiological stimulus-sensitive chimeric transactivator is oxygen-sensitive (sensitive to hypoxia) or glucose-sensitive (sensitive to high glucose levels).

11. The composition of any of claims 1 to 6, wherein the stem cell attracted by said stem cell-attracting chemokine is from an anatomical site selected from the group consisting of bone marrow, peripheral blood, brain, spinal cord, dental pulp, blood vessels, skeletal muscle, epithelia of the skin, epithelia of the digestive system, cornea, retina, liver, and pancreas.

12. The composition of any of claims 1 to 10, wherein said composition is a recombinant viral vector.

13. The composition of any of claims 1 to 12, wherein said composition is a recombinant viral vector selected from the group consisting of an adenovirus, an adeno-associated virus, a herpes simplex virus, a lentivirus, and a retrovirus.

14. The composition of any of claims 1 to 12, wherein said composition is a recombinant adeno-associated viral vector.

15. The composition of any of claims 1 to 11, wherein said composition is a non-viral vector.

16. The composition of any of claims 1 to 11, wherein said composition is a plasmid.

17. A method of targeting a stem cell to a target tissue in an animal subject, the method comprising administering to the target tissue the composition of any of claims 1 to 16.

18. The method of claim 17, wherein the composition is administered to a cell by a delivery method selected from the group consisting of microinjection, electroporation, calcium phosphate transfection, DEAE dextran transfection, polylysine conjugates, receptor-mediated uptake system, liposomal delivery, lipid-mediated delivery system, matrix-impregnated delivery system, microparticle encapsulation, intra-cellular targeting ligand, virion-like particles, and viruses.

19. The method of claim 17 or 18, wherein the target tissue is selected from the group consisting of bone marrow, blood, brain, blood vessels, spinal cord, peripheral nerve, skeletal muscle, cornea, retina, lungs, liver, and pancreas.

20. The method of any of claims 17 to 19, wherein said administering comprises administering the composition to host cells *in vitro* and subsequently administering the host cells to a subject.

21. The method of any of claims 17 to 19, wherein said administering comprises administering the composition to the target tissue *in vivo*.

22. The method of any of claims 17 to 21, wherein following said administering, the nucleic acid sequence encoding the stem cell-attracting chemokine is expressed in the target tissue, and wherein the chemokine attracts endogenous stem cells or endogenous progenitor cells to the target tissue.

23. The method of any of claims 17 to 22, wherein said method further comprises co-administering stem cells to the target tissue.

24. The method of any of claims 17 to 23, wherein said method further comprises administering an agent that causes stem cells to migrate to the target tissue.

25. The method of any of claims 17 to 24, wherein the target tissue is damaged.

26. The method of any of claims 17 to 24, wherein the target tissue is at increased risk of damage.

27. A composition comprising:

(a) a first polynucleotide comprising:

- (1) a tissue-specific promoter,
- (2) a nucleic acid sequence encoding a GAL4 DNA-binding domain,
- (3) a nucleic acid sequence encoding an ODD polypeptide, and
- (4) a nucleic acid sequence encoding a p65 activation domain; and

(b) a second polynucleotide comprising:

- (1) at least two copies of a GAL4 UAS,
- (2) a TATA element, and
- (3) a nucleic acid sequence encoding a stem cell-attracting chemokine.

28. A method of targeting a stem cell to a target tissue in an animal subject, the method comprising administering to the target tissue the composition of claim 27.